REMARKS

With entry of the instant amendment claims 7 - 10 and 14 - 27 are pending. Claims 1 - 6 and 11 - 13 have been canceled, claims 7 and 8 are amended, and claims 14 - 27 are new.

Claims 7 and 8 have been rewritten in independent form incorporating the limitations of now canceled independent claim 1. Claims 14 and 15 recite proteases and subtilisins as the protein of interest. Support may be found, for example, in example 1, page 11, lines 12 - 20, and page 12, lines 4 - 19 of the specification. New claim 16 is an independent claim directed to a method to determine the allergenic potential of an engineered protein. Claims 17 - 25 are dependent on claim 16. New independent claim 26 is directed to a method of using transgenic mice to predict the allergenic response of a human to an engineered protein. Claim 27 is dependent on claim 26. Support for new claims 16 - 27 can be found, for example in example 9 (pages 29 - 30) of the specification.

Applicants believe all pending claims are in form for allowance and allowance of said application is kindly solicited.

Respectfully submitted,

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MARKED-UP VERSION OF EACH AMENDED CLAIM

7.(Once amended) **[The variant of claim 1]** **A variant of a polypeptide of interest comprising a T-cell epitope, wherein said variant differs from said polypeptide of interest by having an altered T-cell epitope such that said variant and said polypeptide produce a different immunogenic response in a individual,** wherein said T-cell epitope is altered **[with]** **by having at least one** amino acid substitution**[s]**.

8.(Once amended) **[The variant of claim 1]** **A variant of a polypeptide of interest comprising a T-cell epitope, wherein said variant differs from said polypeptide of interest by having an altered T-cell epitope such that said variant and said polypeptide produce a different immunogenic response in a individual,** wherein said T-cell epitope is altered by having a terminal portion of said polypeptide of interest comprising said T-cell replaced with a corresponding terminal portion of a homolog of said polypeptide of interest wherein said homolog does not comprise a T-cell **[cell]** epitope identical to said replaced epitope.

Clean Claim Set

7.(Once amended) A variant of a polypeptide of interest comprising a T-cell epitope, wherein said variant differs from said polypeptide of interest by having an altered T-cell epitope such that said variant and said polypeptide produce a different immunogenic response in a individual, wherein said T-cell epitope is altered by having at least one amino acid substitution.

8.(Once amended) A variant of a polypeptide of interest comprising a T-cell epitope, wherein said variant differs from said polypeptide of interest by having an altered T-cell epitope such that said variant and said polypeptide produce a different immunogenic response in a individual, wherein said T-cell epitope is altered by having a terminal portion of said polypeptide of interest comprising said T-cell replaced with a corresponding terminal portion of a homolog of said polypeptide of interest wherein said homolog does not comprise a T-cell epitope identical to said replaced epitope.

9.(reiterated) The variant of claim 8 wherein said variant comprises at least one less T-cell epitope than said polypeptide of interest and said homolog combined.

10.(reiterated) The variant of claim 8 wherein said variant comprises at least two less T-cell epitopes than said polypeptide of interest and said homolog combined.

14.(new) The variant of claim 8, wherein the polypeptide of interest and the homolog of said polypeptide are proteases.

15.(new) The variant of claim 14, wherein said protease is a subtilisin.

16.(new) A method to determine the allergenic potential of an engineered protein comprising the steps of,

a) immunizing a first transgenic mouse with a protein of interest and immunizing a second transgenic mouse with an engineered protein wherein said engineered protein is a variant of said protein of interest and said protein of interest includes a T-cell epitope wherein the variant differs from the protein of interest by having an altered T-cell epitope;

b) collecting serum of said first and said second immunized transgenic mice;

c) measuring the serum for antigen specific immunoglobulins; and

d) comparing the immunogenic response of said variant and said protein of interest wherein the variant and the protein of interest produce a different immunogenic response in said transgenic mice.

17.(new) The method according to claim 16, wherein said protein of interest is an enzyme.

18.(new) The method according to claim 17, wherein said enzyme is a protease.

19.(new) The method according to claim 16, wherein the antigen specific immunoglobulin is IgG.

20.(new) The method according to claim 16, wherein the first transgenic mouse and second transgenic mouse are HLA DR3/DQ2.

21.(new) The method according to claim 20, wherein the HLA DR3/DQ2 transgenic mice have been backcrossed with mice lacking the expression of endogenous I-A class II molecules.

22.(new) The method according to claim 16, wherein said T-cell epitope is altered with amino acid substitutions.

23.(new) The method according to claim 16, wherein said T-cell epitope is altered by having a terminal portion of said protein of interest which includes said T-cell epitope replaced with a corresponding terminal portion of a homolog of said protein of interest wherein said homolog does not comprise a T-cell epitope identical to said replaced T-cell epitope.

24.(new) The method according to claim 16, wherein said immunogenic response produced by the variant is less than the immunogenic response produced by the protein of interest.

25.(new) The method according to claim 16, wherein said immunogenic response produced by the variant is more than the immunogenic response produced by the protein of interest.

26.(new) A method of using transgenic mice to predict the allergenic response of a human to an engineered protein comprising the steps of,

a) immunizing a first transgenic mouse with a protein of interest and immunizing a second transgenic mouse with an engineered protein, wherein said engineered protein is a variant of said protein of interest and the protein of interest includes a T-cell epitope, wherein the variant differs from the protein of interest by having an altered T-cell epitope;

b) collecting serum of the first and the second immunized transgenic mice;

c) measuring the serum for antigen specific immunoglobulins; and

d) comparing the immunogenic response of the variant and the protein of interest, wherein the variant and the protein of interest produce a different immunogenic response in said transgenic mice, and wherein said immunogenic response is predictive of the allergenic response in humans.

27.(new) The method according to claim 26, wherein said protein of interest is a protease.